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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/378,759	08/23/1999	GARY M. FOX	06843.0027-0	9481

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M Paul Barker Esq
Finnegan Henderson Farabow Garrett & Dunner LLP
1300 I Street NW
Washington, DC 20005-3315

EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/378,759	FOX ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29,31 and 36-56* is/are pending in the application.

4a) Of the above claim(s) *28,29,31,36 and 37* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-45 and 47-56* is/are rejected.

7)☐ Claim(s) *38-41, 46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 01/09/04 have been entered in full.

Priority

It is acknowledged that Applicant presented the appropriate amendment in the Divisional Application Transmittal filed August 23, 1999. This amendment will be entered into the specification.

Response to Amendment

Applicant is notified that any outstanding rejection or objection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

Maintained Objections and Rejections:

Claims 38-41 and 46 are objected to because claim 38 encompasses several non-elected patentably distinct inventions (Paper 5, 12/19/03); Applicant is required to delete the non-elected inventions of 38(b) and 38(c).

Applicant argues that because claim 38 is otherwise allowable, then the remaining species of inventions should be examined. This argument has been fully considered but not deemed persuasive. While Applicant is free to structure claims in a variety of formats, the fact remains that the inventions of 38(a), 38(b), and 38(c) are independent and patentably distinct inventions. Although a search of any one of the inventions may overlap that of another, the

search of one could not be relied upon, solely, to provide art that is anticipatory or would render obvious the invention of any other, and to search all inventions would be burdensome.

Contrary to Applicant's assertion, MPEP 809.02(c)(B)(1), cited by Applicant, clearly does not state that once a species is found allowable then the other species must be examined. MPEP 809.02(c)(B)(1) refers to the allowance of a generic claim and species that are fully embraced by the generic claim. No generic claim has been indicated to be allowable. Claim 38 resembles a Markush type claim. If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions, MPEP 803.02. In the instant case, the search of one species could not be relied upon, solely, to provide art that is anticipatory or would render obvious the invention of any other, and to search all species would be burdensome.

Claims 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pasquale EB, Cell Regulation 2(7)523-534, 1991 in view of U.S. Patent No: 4816567, as set forth previously regarding claims 42, 44, and 45. Claims 42-45 simply require that the antibody bind to a sequence as set forth in SEQ ID NO: 11. As set forth previously, many of the antibodies raised against chicken Cek5 would be expected to bind SEQ ID NO: 11 because the two proteins share many more portions of amino acid sequence in common then they do that differ.

As set forth previously, 4816567 teaches that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while

CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success, to make a monoclonal, chimeric, or CDR grafted antibodies according to U.S. Patent No: 4816567 when practicing the invention of Pasquale EB. The motivation to do so is provided by U.S. Patent No: 4816567 wherein in is indicated that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

Applicant's arguments regarding Pasquale, as they relate to claim 42, 44, and 45, have been discussed previously, i.e. that because the two proteins are 95% identical, they contain many more of the same "portions" than those portions that differ between them, and thus most of the antibodies produced against portions of one would be expected to be identical to most of the antibodies raised against the other.

Claims 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iwase et al., Biochem. Biophys. Res. Comm. 194(2)698-705, 1993 in view of U.S. Patent No: 4816567, as set forth in item 10 of Paper 19.

Applicant argues that Iwase et al. never assert that the H1 polypeptide is upregulated and that the mRNA encoding H1 was all that was asserted to be upregulated. Applicant is technically correct, however, one of ordinary skill in the art would read Iwase et al. with the presumption that the polypeptide was also, more likely than not, up regulated as well, and that

the primary focus of Iwase et al. is the potential role of the encoded protein and not the mRNA, e.g. in the Introduction (pg 698) Iwase et al. discuss the role of protein kinases in gastric cancers - thus referring to the protein and not to mRNA. The first sentence of the summary indicates that the focus of this plan of research is to find protein tyrosine kinases, identification of mRNAs encoding the kinases being a first step in this process. Regardless, it is readily apparent that one of ordinary skill in the art would be motivated to make antibodies to the protein sequence disclosed by Iwase et al. to study the role of H1 in the development of gastric cancers, e.g. in the potential for diagnosis and/or treatment, as set forth previously.

Applicant further asserts that Iwase does not teach and would not have suggested using antibodies to detect the Hek5 protein. This argument has been fully considered but not deemed persuasive, as the reverse of this argument has been made previously by Applicant and found to be persuasive – such forming the basis for the withdraw of the rejection under 35 U.S.C. 101 as set forth in the prior Office action dated 9/25/01. In response to this rejection (1/30/02), Applicant asserted the following:

> "Evidence establishes that one skilled in the art would have recognized that antibodies according to claims 38-46 at least can be used to detect cancers that are characterized by overexpression of EPH family members, and to detect the predisposition to such cancers. For example, "it has been shown recently that overexpression of Eph Gilardi-Hebenstreit et al. (1992) Oncogene 7:2499-2506 at page 2504, left column', cited in the Information Disclosure Statement that was filed January 12, 2000 (l.D.S.).This evidence of tumorigenic capacity was borne out in another report, in which the authors studied EPH family member expression levels in human gastric cancers. Specifically, they found that expression of HEKS (also called ERK) mRNA "was extremely higher in Iwase et al. (1993) Biochem. Biophys. cancer tissues than in normal stomach in all cases examined." Res. Comm. 194: 698-705 at page703*, cited in

> the I.D.S. The authors concluded that receptor tyrosine kinase genes, including the HEK5 gene, "play pivotal roles in embryogenesis of stomach and ... the dysregulated expression of these genes have oncogenic potentials in the stomach." Id. at page 704. Another report found that ERK is overexpressed in 75% of gastric cancers tested, suggesting that "ERK plays some significant role in carcinogenesis in the stomach and other tissue." Kiyokawa et al. (1994) Cancer Research 54: 3645-3650 at page 3645, Abstract. A copy of this document is enclosed. Clearly, the correlation between EPH family members and cancer was known at the time of filing. Moreover, antibodies to EPH family members would have been recognized by one skilled in the art as having at least the substantial and credible utility of detecting such cancers and detecting the predisposition to such cancers. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. 101."

Thus, either one of ordinary skill in the art would view it as likely that the antibodies could be used to detect cancer or he would not. For the reasons detailed above by, it has been concluded that he would. Most importantly, the obvious course of action would be to make the claimed antibodies so as to answer the question.

New rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40 and 41 are worded in such a way as to require that the fragment be a chimeric antibody. A fragment of an antibody cannot be, itself, a chimeric antibody or a CDR-grafted antibody. The following claim language is suggested:

40. The antibody or fragment thereof of claim 38, wherein the antibody is a chimeric antibody.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or fragment thereof wherein the antibody is raised against a polypeptide comprising SEQ ID NO: 11 and wherein the fragment binds a polypeptide of SEQ ID NO: 11, does not reasonably provide enablement for fragments that are raised against a polypeptide of SEQ ID NO: 11 or that do not bind a polypeptide of SEQ ID NO: 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claims 47 and 52 recite "An antibody or fragment thereof which is raised against..." Thus, the claims require that the fragment be raised against the polypeptide, which is impossible. Secondly, there is no limitation that requires that the fragment be that part of the antibody that binds to the polypeptide. The specification has failed to teach how to use such an antibody.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 47-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Kirby, J. Immunology, 1992, W.H. Freeman and Company, pages 100-101.

As discussed above claims 47 and 52 do not place any limitations on the claimed antibody fragment, thus the claims encompass the constant region of the antibody (Fc). A fragment consisting of the Fc portion is taught by Kirby.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (571) 272-0871.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

March 25, 2004

YVONNE EYLER, PH D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600